

## **II. REMARKS**

Claims 2 to 14 are pending.

### **A. Regarding the Amendments**

Claim 2 has been amended to be directed to a method of detecting “altered expression of growth differentiation factor-5 (GDF-5) in a subject in need thereof” and to clarify that GDF-5 specific antibody binding is compared to “cells having normal expression of GDF-5”. The amendments are supported, for example, at page 15, lines 10-12; page 18, lines 7-14; and by Examples 2 and 3. Claim 2 has also been amended to further clarify the specificity of a GDF-5 specific antibody “wherein said GDF-5 specific antibody” specifically binds to a GDF-5 polypeptide having an amino acid sequence as set forth in SEQ ID NO: 10 or SEQ ID NO: 13. The amendment is supported, for example, by the previously entered claim and by Figures 2 and 3A, which disclose SEQ ID NO: 10 or SEQ ID NO: 13, respectively. As such, it is submitted that the amendments to claim 2 do not add new matter.

Claim 3 has been amended to recite that the “specimen comprises uterine neoplasm tissue or endometriosis tissue.” The amendment is supported, for example, at page 15, lines 12-14, and by the previously entered claim 3. As such, it is submitted that the amendment to claim 3 does not add new matter.

Claim 4 has been amended to recite that the “specimen comprises skeletal tissue.” The amendment is supported, for example, at page 15, lines 12-14, and by the previously entered claim 3. As such, it is submitted that the amendment to claim 4 does not add new matter.

It is submitted that the amendments do not require a new search or consideration, and that the amendments place the claims in condition for allowance, or in better condition for appeal. As such, it is respectfully requested that the amendments be entered.

**B. Rejections under 35 U.S.C. § 112**

The rejection of claims 2-8, 11 and 12 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement, is respectfully traversed.

The Examiner acknowledges that the specification is enabling for a method of detecting GDF-5 comprising the amino acid sequence shown in Figure 2. It is alleged, however, that the specification, while being enabling for a method of detecting GDF-5 comprising the amino acid sequence shown in Figure 2, does not reasonably provide enablement for a method of detecting a cell proliferative disorder by detecting GDF-5. While the Applicants maintain the traversal of this ground of rejection for reasons previously made of record (see, for example, Applicants response mailed May 27, 2003), the claims have been herein amended in order to expedite prosecution and narrow the issues for appeal. In particular, the currently amended claims are directed at methods of “detecting altered expression of growth differentiation factor-5”. As such, the amendments to the claims have rendered this rejection moot.

Accordingly, it is respectfully requested that this rejection of claims 2-8, 11 and 12 as allegedly lacking enablement be removed.

The rejections of claims 2-8, 11, 12 and 14 under 35 U.S.C. § 112, second paragraph, as indefinite for allegedly failing to particularly point out and distinctly claim the subject matter regarded as the invention is respectfully traversed.

It is alleged in the Office Action that claims 2-8, 11, and 12 are indefinite because it is unclear whether the term “GDF-5”, as recited in the terms “growth differentiation factor-5...cell proliferative disorder,” “GDF-5 specific antibody,” “GDF-5 associated disorder,” and “GDF-5 associated cell proliferative disorder,” is limited to having an amino acid sequence as set forth in SEQ ID NO: 10 or SEQ ID NO: 13. For the reasons set forth above, the claims have been amended and are directed at methods of “detecting altered expression of growth differentiation factor-5.” As such, the terms “growth differentiation factor-5...cell proliferative disorder,” “GDF-5 associated disorder,” and “GDF-5 associated cell proliferative disorder” are not found in

the currently amended claims and the rejection, therefore, is moot with respect to these terms. Regarding the term "GDF-5 specific antibody", claim 2 has been amended to more clearly indicate that an antibody useful in a method of the invention is one that "specifically binds a GDF-5 polypeptide having an amino acid sequence as set forth in SEQ ID NO: 10 or SEQ ID NO: 13." As such, Applicants submit that the subject matter of claims 2-8, 11, and 12 are clearly defined and therefore, respectfully request that this ground of the rejection be removed.

It is also alleged that claim 14 is indefinite because the term "modified cellulose" is not defined and, therefore, the limitations of the element cannot be determined.

Applicants maintain the traversal of this rejection and submit that one skilled in the art, in view of the claimed subject matter (i.e., an immunologic method for detecting a protein), the specification (e.g., page 15, line 18, to page 16, line 10, describing such immunoassays), and the plain meaning of the term, would have known the metes and bounds of modified cellulose useful for the claimed methods. In this regard, Applicants submit that is well known that cellulose is a chemically inert, straight chained polysaccharide composed of linked glucose subunits, with physical properties suitable for binding proteins such as antibodies. It is further submitted that one skilled in the art would have understood that modified cellulose includes a cellulose polysaccharide, obtained from natural sources or synthesized, that has been physically or chemically modified as to affect protein binding properties (see, for example, Exhibit A). Further, examples of cellulose products that have been physically and/or chemically modified and are useful in an immunologic method for detecting a protein are vast and well known in the art (see, for example, Exhibit B; see also, Applicants response mailed May 27, 2003). In fact, one such well known modified cellulose, nitrocellulose, is disclosed in the current specification (see, for example, page 24, lines 13-16). As such, it is submitted that, based on the plain meaning of the term, the current specification, and the knowledge in the art, a skilled artisan would know that the modification of a cellulose intended by the term "modified" includes physical and/or chemical modification as to affect the protein binding properties of the cellulose. Accordingly, it is maintained that one skilled in the art would have known the metes and bounds

of modified cellulose useful for the claimed methods, and it is respectfully requested that this ground of rejection be removed.

It is also alleged that claims 2-8, 11, 12, and 14 indefinite because they recite the term "normal cell" and the term is not defined in the specification or in the claims. It is initially noted that the claim 2 has been amended to require comparison of GDF-5 specific antibody binding to "cells having normal expression of GDF-5." However, in order to be fully responsive to the Office Action, Applicants will address the rejection as applied to the currently amended claims.

It is also stated in the Office Action that the term "normal" is relative and, therefore, indefinite. It is submitted, however, that the mere fact that a term is relative is not dispositive as the its clarity, particularly in the present claim 2, in which the term is used together with the term "altered expression." Applicants further point out that the specification discloses expression patterns of GDF-5 in a variety of adult tissues (Example 2) as well as in embryonic tissues (Example 3). As such, one skilled in the art would recognize that GDF-5 is normally expressed primarily in adult uterine tissue and at lower levels in other adult tissues, including placenta, brain, thymus, lung, kidney, and adrenal gland, and GDF-5 is normally expressed primarily in the skeletal system in embryos. In view of the specification, numerous examples of cells having normal expression of GDF-5 in adult and embryonic tissues would be apparent to the skilled artisan such that the metes and bounds of the claimed subject matter clearly would be known. As such, it is respectfully requested that this ground of rejection be removed.

In view of the amendments, and for the reasons set forth above, it is submitted that one skilled in the art, reading the claims, would know the metes and bounds of the claimed subject matter. Accordingly, it is respectfully requested that the rejections of claims 2-8, 11, 12, and 14 under 35 U.S.C. § 112, second paragraph, be removed.

In re Application of:  
Lee and Huynh  
U.S. Serial No. 09/880,708  
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In view of the amendments and the above remarks, it is submitted that the claims are in condition for allowance, and a notice to that effect respectfully is requested. The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this application.

Please charge any additional fees, or make any credits, to Deposit Account No. 50-1355.

Respectfully submitted,

Dated: \_\_\_\_\_

11/11/03



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**Enclosure: Exhibit A, B**